CLAIMS

1. A polypeptide dendrimer having: i) a multifunctional core moiety; ii) an exterior of closely spaced groups constituting the terminals of branched polypeptide chains (monodendrons) radially attached to the core that, in turn, form iii) interior layers (generations) of short peptide branching units (propagators) with characteristic hollows and channels where each propagator contains a trifunctional aminoacid whose asymmetric carbon (the propagator branching point) is connected to two equal-length arms bearing identical terminal reactive groups and to a third arm (the propagator stem) bearing an activatable functional group,
represented by formula (I):

$K(-L)_p-M$ (I) wherein

K is a multifunctional core moiety,
L is a polypeptide monodendron,
p is the number of polypeptide monodendrons irradiating from the core moiety and M represents the outermost ramifications of the dendrimer;

2. A polypeptide dendrimer of claim 1 where said K is represented by formula (II):

$X-(CH_2)_n-X^1$ (II)

wherein $X=X^1$ or $X\neq X^1$, and X, X^1 are NH or CO or S;

3. A polypeptide dendrimer of claim 1 where said K is represented by formula (III):

$Y[-(CH_2)_n-Z]_i$ (III)

wherein Y=C or Y=N; Z is NH or S or Cl or Br or I or a maleimide residue, n=1-6 and i=3,4;

4. A polypeptide dendrimer of claim 1 where said K is represented by formula (IV):

$$X-CH(R)-CO[-NH-CH(R)-CO]_n-NH-CH(R)-COOR^1 \quad (IV)$$

wherein R is $(CH_2)_m-X^1$, m=1-5, R^1 is methyl or ethyl or butyl or isopropyl, $X=X^1$ or $X\neq X^1$, and X, X^1 are NH or CO or S and n=1-6;

5. A polypeptide dendrimer of claim 1 where said L is the single monodendron whose propagators are repres nted by formula (V):

$$-CO-CH(R^2)-(CH_2)_n-NR^3- \quad (V)$$

wherein R^2=H or the side-chain of natural or synthetic aminoacids, and their derivatives; R^3=H or a linear hydrocarbon radical optionally substituted with OH or SH or Cl or Br; R^2-CH$(CH_2)_n$-NR^3 is a 5 or 6 atoms ring, and n=0-6;

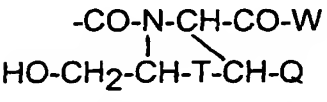
6. A polypeptide dendrimer of claim 1 where said L is the single monodendron whose propagators are represented by formula (VI):

$$-CO-CH(R^2)-CO-N(R^3)-(CH_2)_m-N(R^3) \qquad (VI)$$

wherein R^2 and R^3 have the meaning seen in claim 5 and m=1-6;

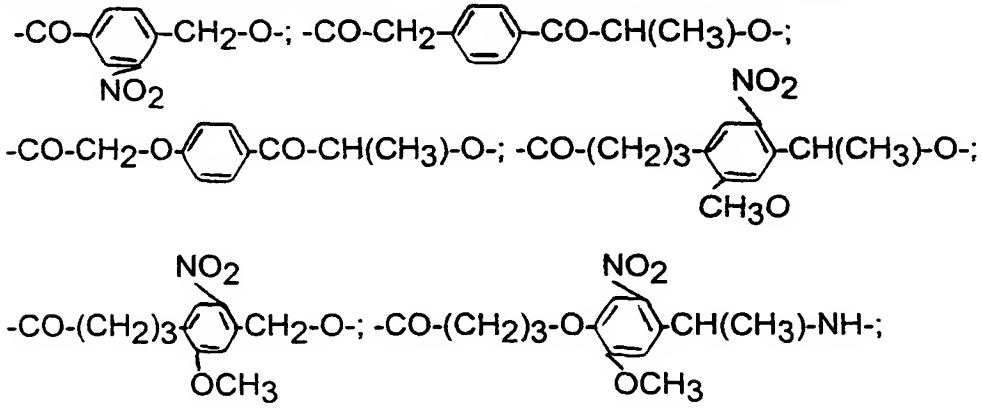
7. A polypeptide dendrimer of claim 1 where said L is the single monodendron whose propagators are represented by one of the residues:

-CO-CH_2-NH-NH-; or -CO-CH(R^2)-O-; or -CO-CH_2-O-N=CH-CO-; or -CO-CH(R^2)-$(CH_2)_n$-S-CH_2-CO-W; or -CO-NH-CH(CH_2-SH)-CO-W or



wherein W=-N(R^3)-$(CH_2)_m$-NR^3, Q=H or -CH_3; T is O or S whereas R^2, R^3 and m have the meaning seen in claim 5;

8. A polypeptide dendrimer of claim 1 where said L is the single monodendron whose propagators are represented by one of the residues:



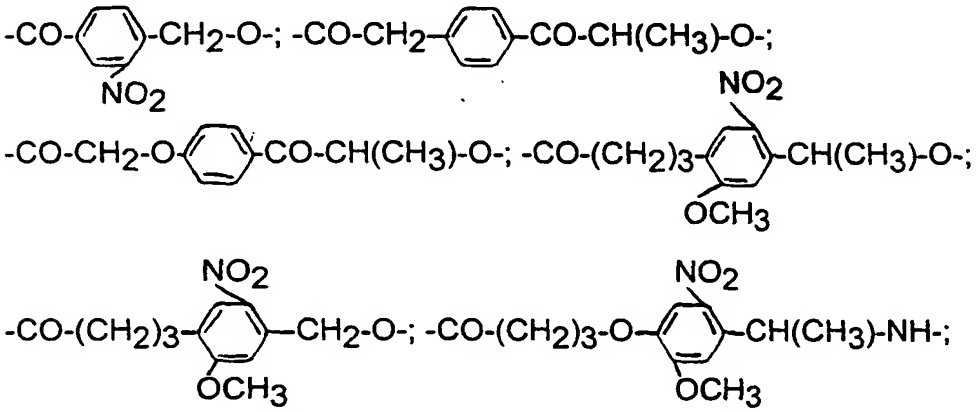
9. A polypeptide dendrimer of claim 1 where said p is 1 or 2 or 3 or 4;

10. A polypeptide dendrimer of claim 1 where said M is the residue represented by formula (VII):

$$-Aq-B(Ar)-C-Ar[Aq-B(Ar)-C-Ar[Aq-B(Ar-D)-C-Ar-D]_2]_2 \qquad (VII)$$

wherein A=-CO-CH(R^2)-(CH_2)n-NR^3, R^3 and n have the meaning seen in claim 5, q=1-6, r=1-4 and R^2, in addition to the meaning seen in claim 5, is a natural or

synthetic trifunctional aminoacid; B is -CO-CH[-(CH_2)n-X^1]-X, with X=X^1 or X≠X^1; X and X^1 are NH or CO or S; n=1-5; C=A or C=-CO(CH_2)n-NH- or -(CH_2)n-S- with n=1-6 or C is one of the residues:



D is a residue represented by formulae (VIII)-(XI):

-Aq-B(Ar-E)-C-Aq-E (VIII)

-Aq-B(Ar)-C-Aq[Aq-B(Ar-E)-C-Aq-E]$_2$ (IX)

-Aq-B(Ar)-C-Aq[Aq-B(Ar)-C-Aq-[Aq-B(Ar-E)-C-Aq-E]$_2$]$_2$ (X)

-Aq-B(Ar)-C-Aq[Aq-B(Ar)-C-Aq-[Aq-B(Ar)-C-Aq[Aq-B(Ar-E)-C-Aq-E]$_2$]$_2$]$_2$ (XI)

wherein A, B, C, q ed r have the meaning seen above , and E is represented by formulae (XII) and (XIII):

-Aq-B(Ar-P)-C-Aq-P^1 (XII)

-Aq-B(Ar)-C-Aq[-Aq-B(Ar-P)-C-Aq-P^1]$_2$ (XIII)

wherein A, B, C, q and r have the meaning seen above, P=P^1 or P≠P^1, P and P^1 being H or a linear hydrocarbon radical optionally substituted with one or more linear or branched alkyl groups, acyl, aminoacid, peptide, nucleotide, oligonucleotide, saccharide, oligosaccharide, protein, monoclonal antibody, polyethyleneglycol containing 10-400 -CH_2-CH_2-O- repeats, lipid, enzyme, metal ligand or their synthetic analogues and derivatives;

11. A polypeptide dendrimer of claims 1-10 wherein the two-dimensional molecular diameter of the dendrimers is in the range from about 10 to 100 nm.

12. The dendrimer $_2$(2(2(H-Gly-Orn-Gly-Gly)Gly-Orn-Gly-Gly)Gly-Orn-Gly-Gly)Gly-Orn-Gly-Gly-HN-CH_2-CH_2-NH-Gly-Gly-Orn-Gly(Gly-Gly-Orn-Gly(Gly-Gly-Orn-Gly(Gly-Gly-Orn-Gly-H)$_2$)$_2$)$_2$.

13. The dendrimer $_2$(2(2(2(H-Gly-Orn-Gly-Gly)Gly-Orn-Gly-Gly)Gly-Orn-Gly-

Gly)Gly-Orn-Gly-Gly)Gly-Orn-Gly-Gly-HN-CH_2-CH_2-NH-Gly-Gly-Orn-Gly(Gly-Gly-Orn-Gly(Gly-Gly-Orn-Gly(Gly-Gly-Orn-Gly(Gly-Gly-Orn-Gly-H)$_2$)$_2$)$_2$)$_2$.

14. The dendrimer $_2$(2(2(2(2(H-Gly-Orn-Gly-Gly]Gly-Orn-Gly-Gly)Gly-Orn-Gly-Gly)Gly-Orn-Gly-Gly)Gly-Orn-Gly-Gly)Gly-Orn-Gly-Gly-HN-CH_2-CH_2-NH-Gly-Gly-Orn-Gly(Gly-Gly-Orn-Gly(Gly-Gly-Orn-Gly(Gly-Gly-Orn-Gly(Gly-Gly-Orn-Gly(Gly-Gly-Orn-Gly-H)$_2$)$_2$)$_2$)$_2$)$_2$.

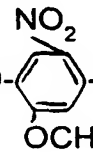
15. The dendrimer $_2$(2(2(2(2(2(H-Gly-Orn-Gly-Gly)Gly-Orn-Gly-Gly)Gly-Orn-Gly-Gly)Gly-Orn-Gly-Gly)Gly-Orn-Gly-Gly)Gly-Orn-Gly-Gly)Gly-Orn-Gly-Gly-HN-CH_2-CH_2-NH-Gly-Gly-Orn-Gly(Gly-Gly-Orn-Gly(Gly-Gly-Orn-Gly(Gly-Gly-Orn-Gly(Gly-Gly-Orn-Gly(Gly-Gly-Orn-Gly-H)$_2$)$_2$)$_2$)$_2$)$_2$.

16. The dendrimer $_2$(2(2(2(2(2(H-Gly-Orn-Gly-Gly)Gly-Orn-Gly-Gly)Gly-Orn-Gly-Gly)Gly-Orn-Gly-Gly)Gly-Orn-Gly-Gly)Gly-Orn-Gly-Gly)Gly-Orn-Gly-Gly-HN-CH_2-CH_2-NH-Gly-Gly-Orn-Gly(Gly-Gly-Orn-Gly(Gly-Gly-Orn-Gly(Gly-Gly-Orn-Gly(Gly-Gly-Orn-Gly(Gly-Gly-Orn-Gly(Gly-Gly-Orn-Gly-H)$_2$)$_2$)$_2$)$_2$)$_2$)$_2$.

17. The dendrimer N{-CH_2-CH_2-NH-CO-CH(-CH_2-phenyl)-NH-Gly-Gly-Gly-Orn-Gly[Gly-Gly-Gly-Orn-Gly[Gly-Gly-Gly-Orn-Gly[Gly-Gly-Gly-Orn-Gly-H]$_2$]$_2$]$_2$}$_3$.

18. The dendrimer N{-CH_2-CH_2-NH-CO-CH(-CH_2-phenyl)-NH-Gly-Gly-Gly-Orn-Gly[Gly-Gly-Gly-Orn-Gly[Gly-Gly-Gly-Orn-Gly[Gly-Gly-Gly-Orn-Gly[Gly-Gly-Gly-Orn-Gly-H]$_2$]$_2$]$_2$]$_2$}$_3$.

19. The dendrimer N{-CH_2-CH_2-N(-CO-)-CO-CH-S-CH_2-CH(COOH)-NH-



-CO(CH_2)$_3$-O-(-CH(CH_3)-NH-Gly-Gly-Gly-Orn-Gly[Gly-Gly-Gly-Orn-Gly[Gly-Gly-Gly-Orn-Gly[Gly-Gly-Gly-Orn-Gly[Gly-Gly-Gly-Orn-Gly[Gly-Gly-Gly-Orn-Gly-H]$_2$]$_2$]$_2$]$_2$]$_2$]$_2$}$_3$.

20. The polypeptide dendrimers of claims 12-19 wherein the NH_2 terminals are acetylated.

21. A polypeptide dendrimer of claim 1 wherein at least one bioactive or marker molecule is covalently linked to the surface of the same.

22. A polypeptide dendrimer of claim 21 where the bioactive molecule is selected in the group comprising an aminoacid, a peptide, a protein, a nucleotide, an oligonucleotide, a lipid, a saccharide, an oligosaccharide, and a small organic molecule and their synthetic analogues and derivatives.

23. A polypeptide dendrimer of claim 21 where the bioactive molecule is selected in the group comprising drugs, cellular receptor ligands, bacterial, viral and parasite antigens and gene-therapy compounds.

24. A polypeptide dendrimer of claim 21 where the marker molecule is a diagnostic imaging contrast agent.

25. A polypeptide dendrimer of claim 1 where the bioactive molecule is entrapped in the same.

26. A polypeptide dendrimer of claim 25 where the bioactive molecule is selected in the group comprising an aminoacid, a peptide, a protein, a nucleotide, an oligonucleotide, a lipid, a saccharide, an oligosaccharide, and a small organic molecule and their synthetic analogues and derivatives.

27. A polypeptide dendrimer of claim 25 where the bioactive molecule is selected in the group comprising drugs, cellular receptor ligands, bacterial, viral and parasite antigens and gene-therapy compounds.

28. A polypeptide dendrimer of claim 27 where the bioactive molecules are anticancer drugs.

29. A polypeptide dendrimer of claim 27 where the bioactive molecules are antibiotics.

30. A polypeptide dendrimer of claim 27 where the bioactive molecules are antiviral substances.

31. A process for production of the polypeptide dendrimers of claim 1 characterized by the following steps:

i) synthesis of core moieties with at least two reactive functional groups;

ii) divergent synthesis on solid-phase of polypeptide monodendrons with temporarily or permanently protected terminals;

iii) covalent condensation of polypeptide monodendrons to core moieties;

32. A process for production of polypeptide dendrimers of claim 1 characterized by the following steps:

i) synthesis of core moieties with at least two reactive functional groups;
ii) covalent condensation to the core moieties of polypeptide monodendrons of generation 1-3 with temporarily protected terminals to obtain the corresponding protected dendrimers;
iii) after protecting groups removal, repeated condensations of polypeptide monodendrons to the dendrimer reactive terminals to obtain the desired final dendrimers.

33. A process for entrapping into the polypeptide dendrimers of claim 1 bioactive substances and drugs with molecular weights lower than 1,000 Da, characterized by the following steps:
(a) adding suitable amounts of polypeptide dendrimers to a concentrated or saturated solution of said molecules and
(b) precipitating the loaded polypeptide dendrimer after 24 h incubation at room temperature in a large volume of a precipitant.

34. A process for entrapping into the polypeptide dendrimers of claim 1 bioactive substances and drugs with molecular weights higher than 1,000 Da, characterized by the selective chemical ligation of polypeptide monodendrons, in aqueous buffers, to the core moieties in the presence of said molecules.

35. A process for the selective chemical ligation of bioactive substances and drugs to the internal functional groups of the polypeptide dendrimers of claim 1, in aqueous buffers, after loading the dendrimer carrier by diffusion.

36. Use of polypeptide dendrimers of claim 1 as unimolecular carriers of bioactive molecules wherein at least one bioactive or marker molecule is covalently linked to the surface of the same.

37. Use of polypeptide dendrimers according to claim 36 where the bioactive molecule is selected in the group comprising an aminoacid, a peptide, a protein, a nucleotide, an oligonucleotide, a lipid, a saccharide, an oligosaccharide, and a small organic molecule and their synthetic analogues and derivatives.

38. Use of polypeptide dendrimers according to claim 36 where the bioactive molecule is selected in the group comprising drugs, cellular receptor ligands, bacterial, viral and parasite antigens and gene-therapy compounds.

39. Use of polypeptide dendrimers according to claim 36 where the marker

molecule is a diagnostic imaging contrast agent.

40. Use of polypeptide dendrimers of claim 1 as unimolecular carriers of bioactive molecules wherein the bioactive molecule is entrapped into the same.

41. Use of polypeptide dendrimers according to claim 40 where the bioactive molecule is selected in the group comprising an aminoacid, a peptide, a protein, a nucleotide, an oligonucleotide, a lipid, a saccharide, an oligosaccharide, and a small organic molecule and their synthetic analogues and derivatives.

42. Use of polypeptide dendrimers according to claim 40 where the bioactive molecule is selected in the group comprising drugs, cellular receptor ligands, bacterial, viral and parasite antigens and gene-therapy compounds.

43. Use of polypeptide dendrimers according to claim 40 where the bioactive molecules are anticancer drugs.

44. Use of polypeptide dendrimers according to claim 40 where the bioactive molecules are antibiotics.

45. Use of polypeptide dendrimers according to claim 40 where the bioactive molecules are antiviral substances.

46. Compositions with pharmaceutically acceptable excipients wherein the polypeptide dendrimers of claim 1 are the unimolecular carriers of bioactive or marker molecules covalently linked at the surface of the same.

47. Compositions with pharmaceutically acceptable excipients wherein the polypeptide dendrimers of claim 1 are the unimolecular carriers of bioactive molecules entrapped into the same.

ADD A1